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Use Data and Details to Convince Site Leadership to Add Staff

By James Miessler

Sites can add depth to their research teams by creating specialized positions and potentially free up existing staff to take on more trials. The challenge is in site managers or directors convincing site leadership — typically vice presidents — that the gains outweigh the costs.

Making the case to budget-conscious site leaders requires strong data and a compelling argument that clearly shows the return on investment, one research director says.

Positions such as regulatory staff, data specialists, research pharmacists and study startup/recruitment specialists can add capabilities and flexibility to a site that is struggling to keep up with its trials, said Suzanne Rose, director of Stamford Hospital's Office of Research. But that's not always a convincing sales pitch.

"It's hard to justify bringing in positions that don't always have a dollar sign attached to them. Try to think outside the box with your organization," Rose advised attendees at the recent Association of Clinical Research Professionals annual conference. "Really find that way you can identify with your leadership on different types of positions to say, 'this position is really needed for compliance reasons, this position we can tie back to revenue directly or indirectly,'" she said.

To propose adding a regulatory specialist to the staff, for instance, emphasize

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Ask the Experts: Listing Trial Staff and Others on the Statement of Investigator

The FDA's Good Clinical Practice Program (GCPP) fields dozens of questions each year related to completing and signing the Form FDA 1572 — Statement of Investigator. The following are some of the questions GCPP has received recently with answers from the program's senior analysts.

Question: *We see inconsistency from industry sponsors on whether clinical research coordinators should be listed in Section 6 of Form 1572. What is the FDA's current thinking on this?*

Answer: Many people do not realize that one of the main purposes of the 1572 is to provide the sponsor with information about the clinical site and investigator qualifications that will enable the sponsor to establish and document that the investigator and site are qualified to conduct the study.

Section 6 asks for the "Names of the sub-investigators (e.g., research fellows, residents, associates) who will be assisting the investigator in the conduct of the investigation(s)." "Sub-investigator" is indirectly defined in the drug and biologics regulations (21 CFR 312.3(b):

"Investigator means an individual(s) who actually conduct(s) a clinical investigation (i.e., under whose immediate direction the drug or biologic is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader

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Clinical Trials Day

WCG salutes clinical trial professionals and participants as we celebrate Clinical Trials Day on May 20.

Upcoming Events

17 MAY — WEBINAR
Three Data Trends to Consider Now When Developing Your Decentralized Clinical Trial Strategy

19 MAY — WEBINAR
The Great Resignation: Its Impact on Clinical Research & Where We Go From Here

[VIEW ALL EVENTS]

Industry Briefs

FDA Offers Advice on Human Radiolabeled Mass Balance Studies

Human radiolabeled mass balance studies are the most direct way of gathering quantitative data on a drug's absorption, distribution, metabolism and excretion (ADME) in the human body, according to draft guidance the FDA issued in early May.

The FDA 11-page guidance says such studies should generally be carried out for all new molecular entities.

The guidance's considerations for designing mass balance studies and reporting their results covers areas including study design, participants, radioactivity dose, investigational drug dose, route of administration and formulation of the drug, sample collection/handling and determination of absolute bioavailability for oral drugs, among others.

However, there are some situations in which they may not be advised "unless clinical concerns suggest otherwise," including for:

- Drugs that have acceptable mass balance study results already available;
- Drugs that have known metabolism and elimination pathways based on basic pharmacology and nonclinical ADME information (such as monoclonal antibodies, endogenous substances and analogs);
- Drugs whose doses are nearly fully recovered as the unchanged parent drug in the urine; and
- Drugs with little to no systemic exposure.

Alternatives suggested by the guidance include animal mass balance studies, metabolic profiling using qualitative techniques, urine collection in phase 1 trials and in vitro assessments to characterize the drug's ADME, but these should be discussed with the agency before being used.

Mass balance studies should be done early and prior to starting late-phase clinical trials at the latest so that data can be collected to inform the overall development program, the guidance says.

Comments on the draft guidance are due by Aug. 3.

Read the full guidance here: https://bit.ly/3L5Mx44.

Abbott Joins Women's Advocacy Group to Launch Researcher Diversity Program

In an effort to increase the diversity of physicians engaging in clinical research, Abbott and Women as One, a nonprofit, have launched a program to train female and underrepresented physicians to conduct clinical trials.

The training program, dubbed CLIMB Research, offers physicians a blend of case reviews, guest lectures, group discussions and lessons on good clinical practice, protocol oversight, IRB reporting, safety management and practical applications in the clinical research environment.

The program is initially focused on interventional cardiology and is open to women, Black, Hispanic, Native American, Asian, South Asian and nonbinary cardiologists, the pair said.

Learn more about the program here: https://bit.ly/3N2vRMm.

Data Point

Demographic Reporting of Trials in the EU v. the U.S.

	Pivotal trials supporting approval of new medicines in the EU (2007 – 2017)		Pivotal trials supporting FDA approvals (2007 – 2017)	
	n	*Percent*	*n*	*Percent*
Gender demographics	649	78.8%	679	89.7%
Racial demographics	510	61.9%	551	72.8%
Ethnicity demographics	229	27.8%	278	36.7%

Source: Tufts Center for the Study of Drug Development

Convince Site Leadership

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that such a position increases regulatory compliance both with the IRB and the FDA and note that such staff can free up other staff — especially CRCs — to focus on accelerating trial startup and improving enrollment, Rose said. And be sure to let leadership know — especially if they want to be able to link the hire to site revenue — that regulatory personnel can reduce about 25 percent of CRC burdens.

"If you say … coordinators can then take on another study, another two studies because they have regulatory support, then you can say that there's revenue that comes in … that you can tie back to the regulatory personnel," she said.

New data specialists/managers also can relieve the burden on CRCs. Stamford uses them to promptly collect and upload data, maintain the clinical trial management system and develop reports, forms and templates as necessary. This role can serve as a multidepartment position as well, supporting onsite visits and remote monitoring, pitching in as a backup research coordinator and helping to process and ship research specimens.

Always include this position in trial budgets, Rose advised. In her experience, sponsors will reimburse sites about 80 percent of the time, understanding the benefits of having data specialists on staff.

Stamford employs study startup/patient recruitment specialists for a variety of tasks, including completing feasibility questionnaires and leading site initiation visits, finding promising trials, reviewing/presenting protocols and serving as the first point of contact between the research team and sponsors/CROs. They're also responsible for keeping detailed records of startup timelines, preselecting potential participants and managing phone calls as well as supporting the development and upkeep of the site's social media advertisements.

"Be as specific as possible. General statements such as 'we need more staff' do not adequately explain the business need, nor do they portray the effect on operational performance."

—Sandy Smith, senior VP for clinical solutions and strategic partnerships, WCG

The selling points for this position, she said, are that a dedicated recruiting manager can increase enrollment by 25 percent on average, which is particularly compelling for sites struggling to sign up participants. Rose noted that 20 to 25 percent of trials close because they fail to meet enrollment goals. One-third of a CRC's time can be tied up by recruitment, and study startup can take 10 to 15 percent of their time away from enrollment and patients.

Adding a site pharmacist also takes several tasks off CRCs' plates, especially investigational drug storage and inventory. Stamford uses their pharmacists to maintain the pharmacy binder, instruct staff on all of the trial drugs' aspects, help avoid drug compliance problems and even assist with regulatory tasks when needed, including checking informed consent compliance and managing a checklist for trial eligibility.

The pharmacist position also should be included in the trial budget. Justify it by outlining any drug compliance issues the hire can help prevent, including lost drugs, temperature excursions and incorrect dosing that can cost sites money or, worse, harm patients. Rose noted that problems with investigational drugs can cost sites hundreds of thousands of dollars over time.

In addition to presenting the benefits of a new hire, it's important to outline the ramifications of not having a position filled, Sandy Smith, senior vice president for clinical solutions and strategic partnerships at WCG, told *CenterWatch Weekly*. Use measurable details and include a commercial angle; for example, if not having certain personnel would impact data entry timelines, share how many days late data entry would be and how it would affect the site's ability to open more trials.

"Be as specific as possible. General statements such as 'we need more staff' do not adequately explain the business need, nor do they portray the effect on operational performance both quantitative and qualitative," Smith said.

Ask the Experts

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of the team. 'Sub-investigator' includes any other individual member of that team."

Again, the purpose of Section 6 is to capture information about those individuals who will play a key role in the collection and interpretation of data as well as in the conduct of the study itself. Hospital staff, including nurses, residents or fellows, and office staff who provide ancillary or intermittent care but who do not make direct and significant contribution to the data are generally not meant to be listed. A general statement regarding the participation of staff residents on rotation can be included in Section 6.

Whether to list an individual depends on the level of responsibility the individual has in the conduct of the study and in the evaluation of information obtained during the study. If the individual in question has significant study-related duties (e.g., explaining the study to subjects, qualifying the study subjects), then the person should be listed on the 1572. If the individual merely ensures and observes that, for example, a consent form is signed by the subject after the principal investigator has explained the study and qualified the subject, then this person would not have to be listed.

Note: If a research coordinator is performing critical study functions and collecting and evaluating some study data, the coordinator should be listed on the 1572. If the research coordinator is only transcribing data and maintaining study files, the coordinator does not need to be listed.

Question: *The sponsor of our phase 1 trial has added to the protocol an assessment performed by a specialist to investigate a specific adverse event that is occurring. The sponsor has contracted with a specialist from one of the trial's sites to be part of its medical monitor team that evaluates the events reported by the sites and provides guidance to them (e.g., discussion about available treatments and mechanism of action of the study drug that causes the toxicity).*

As this specialist has continued to see the active patients at one of the sites, the CRO asked the site to add this specialist to the site team and collect the proper documentation (i.e., financial disclosure form, updated 1572 form and all site logs). However, the site considers the specialist an ancillary physician to the trial (the specialist is not even part of the research institution responsible for the trial) and believes it would not need to add her/him to the site team list and update/collect any documentation. This specialist has a financial interest in the research as the sponsor has paid for his/her services.

Is the site correct or should it add the specialist to the Form 1572?

Answer: From the limited information in your email, it appears the specialist should be listed on the Form 1572, especially if this person is evaluating the toxicity as an adverse event. If this person is listed on the 1572, the other forms should follow.

Please note that a site delegation log is not required by FDA regulations; however, it is recommended by the ICH E6(R2) — Good Clinical Practice guideline, although the guidance does not provide details as to who should be listed. The FDA's guidance document on the supervisory responsibilities of clinical investigators speaks to the need for delegation of trial tasks only to qualified personnel; the agency therefore considers it important to document what trial task was delegated to whom.

As to who should be included on the delegation log — it would be anyone who has an essential role in the conduct of the trial. For example, if blood draws are essential to either the timing, dosage or follow-up of participants, the identity of the lab tech assigned to the trial may also be important to capture.

Question: *We have a protocol that requires audiology and neurological tests. These tests will be performed by external facilities that will be listed in Section 4 of the Form 1572. These tests are related to the safety endpoints of the study, one of which is primary, but they are routine tests for these departments and are not trial-specific.*

Should staff of an external facility — such as an audiologist or neurologist — who perform these tests be designated as sub-investigators and listed in Section 6?

Answer: As to whether you have to list the names of the audiologist(s) or neurologist(s) as sub-investigator(s) in Section 6, this is a sponsor decision. In general, if the tests being performed at the audiologist and neurologist offices are standard routine tests and there may be a few different personnel who may perform the tests, you could consider not listing all such names in Section 6 but perhaps choose to list them in the trial records instead. However, the decision about whether to list a specific audiologist(s) and/or neurologist(s) in Section 6 is a matter of judgment that depends on the contribution that the individual makes to the trial. Discussing your question with the appropriate staff at your sponsor company should help you to decide the best path forward.

Drug & Device Pipeline News

Company	Drug/Device	Medical Condition	Status
Trials Authorized			
Cue Biopharma	CUE-102	Wilms' tumor 1 (WT1)-expressing cancers	IND approved by the FDA
Elpiscience Biopharmaceuticals	ES014	Advanced solid tumors	IND approved by the FDA
Regulus Therapeutics	RGLS8429	Autosomal dominant polycystic kidney disease	IND approved by the FDA
Neogene Therapeutics	NT-125	Advanced solid tumors	Clinical trial authorized by the Dutch regulatory authory
ReAlta Life Sciences	RLS-0071	Severe asthma	Approval for a phase 1b trial granted by Germany's regulatory authority
Spine BioPharma	SB-01 for injection	Chronic low back pain caused by degenerative disc disease	Study may proceed letter issued by the FDA
Zylorion Health	Almond Therapy	Treatment-resistant depression	Approval for a phase 2 trial granted by Canada's regulatory authority

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Drug & Device Pipeline News

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Company	Drug/Device	Medical Condition	Status
Trials Initiated			
Arcellx	ACLX-001	Relapsed or refractory multiple myeloma	Initiation of phase 1 trial
Bio-Thera Solutions	BAT7104	Advanced solid tumors	Initiation of phase 1 trial in Australia
Zhimeng Biopharma	CB03	Refractory epilepsy	Initiation of phase 1 trial
Immatics	IMA401	Advanced solid tumors	Initiation of phase 1 trial
Imago Biosciences	Bomedemstat in combination with atezolizumab	Extensive-stage small-cell lung cancer	Initiation of phase 1/2 trial
Myeloid Therapeutics	MT-101	Peripheral T-cell lymphoma	Initiation of phase 1/2 trial
Eledon Pharmaceuticals	Tegoprubart	IgA nephropathy	Initiation of phase 2a trial
Intercept Pharmaceuticals	Obeticholic acid and bezafibrate	Primary biliary cholangitis	Initiation of phase 2 trial
Sen-Jam Pharmaceutical	SJP-002C	COVID-19	Initiation of phase 2 trial
Zenith Epigenetics	ZEN-3694 plus talazoparib	Triple negative breast cancer	Initiation of phase 2b trial
Anthos Therapeutics	Abelacimab	Cancer-associated thrombosis	Initiation of phase 3 trial
Faraday Pharmaceuticals	FDY-5301	Anterior ST-segment elevation myocardial infarction	Initiation of phase 3 trial
Approvals			
Eli Lilly	Olumiant (baricitinib)	COVID-19 in certain hospitalized adults requiring various degrees of oxygen support	Approved by the FDA

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